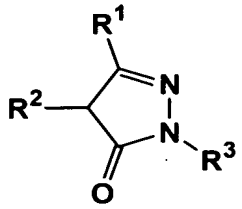
AMENDMENTS TO THE CLAIMS

This listing of claims replaces all prior versions, and listings, of claims in the application.

1. (Original) A blood-brain barrier disruption inhibitor which comprises as an active ingredient a pyrazolone derivative represented by the following formula (I) or a physiologically acceptable salt thereof, or a hydrate thereof or a solvate thereof:



(I)

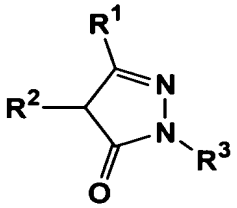
wherein R^1 represents a hydrogen atom, an aryl group, a C_{1-5} alkyl group, or a C_{3-6} (total carbon number) alkoxycarbonylalkyl group; R^2 represents a hydrogen atom, an aryloxy group, an arylmercapto group, a C_{1-5} alkyl group or a C_{1-3} hydroxyalkyl group; or R^1 and R^2 are combined with each other to represent C_{3-5} alkylene group; and R^3 represents a hydrogen atom, a C_{1-5} alkyl group, a C_{5-7} cycloalkyl group, a C_{1-3} hydroxyalkyl group, a benzyl group, a naphthyl group, a phenyl group, or a phenyl group substituted with the same or different 1 to 3 substituents selected from the group consisting of a C_{1-5} alkyl group, a C_{1-5} alkoxy group, a C_{1-3} hydroxyalkyl group, a C_{2-5} (total carbon number) alkoxycarbonyl group, a C_{1-3} alkylmercapto group, a C_{1-4} alkylamino group, a C_{2-8} (total carbon number) dialkylamino group, a halogen atom, a trifluoromethyl group, a carboxyl group, a cyano group, a hydroxyl group, a nitro group, an amino group and an acetamide group.

2. (Original) The blood-brain barrier disruption inhibitor according to claim 1 which has an action of inhibiting increases in permeability of the blood-brain barrier.

3. (Currently Amended) The blood-brain barrier disruption inhibitor according to claim 1 ~~or 2~~ which has an action of inhibiting increases in the amount of inflammatory cytokines in spinal fluid.

4. (Currently Amended) The blood-brain barrier disruption inhibitor according to ~~any of claims 1 to 3~~ claim 1 wherein the pyrazolone derivative represented by the formula (I) is 3-methyl-1-phenyl-2-pyrazolin-5-one.

5. (Original) A medicament for prevention and/or treatment of multiple sclerosis, meningitis, cerebritis or brain abscess, which comprises as an active ingredient a pyrazolone derivative represented by the above-described formula (I) or a physiologically acceptable salt thereof, or a hydrate thereof or a solvate thereof:

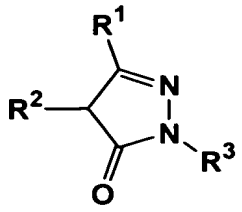


(I)

wherein R^1 represents a hydrogen atom, an aryl group, a C_{1-5} alkyl group, or a C_{3-6} (total carbon number) alkoxycarbonylalkyl group; R^2 represents a hydrogen atom, an aryloxy group, an arylmercapto group, a C_{1-5} alkyl group or a C_{1-3} hydroxyalkyl group; or R^1 and R^2 are combined with each other to represent C_{3-5} alkylene group; and R^3 represents a hydrogen atom, a C_{1-5} alkyl group, a C_{5-7} cycloalkyl group, a C_{1-3} hydroxyalkyl group, a benzyl group, a naphthyl group, a phenyl group, or a phenyl group substituted with the same or different 1 to 3 substituents selected from the group consisting of a C_{1-5} alkyl group, a C_{1-5} alkoxy group, a C_{1-3} hydroxyalkyl group, a C_{2-5} (total carbon number) alkoxycarbonyl group, a C_{1-3} alkylmercapto group, a C_{1-4} alkylamino group, a C_{2-8} (total carbon number) dialkylamino group, a halogen atom, a trifluoromethyl group, a carboxyl group, a cyano group, a hydroxyl group, a nitro group, an amino group and an acetamide group.

6. (Original) The medicament according to claim 5 wherein the pyrazolone derivative represented by the formula (I) is 3-methyl-1-phenyl-2-pyrazolin-5-one.

7. (Original) A method for inhibiting a blood-brain barrier disruption which comprises a step of administering to mammals such as a human, an effective amount of a pyrazolone derivative represented by the formula (I) or a physiologically acceptable salt thereof, or a hydrate thereof or a solvate thereof:



(I)

wherein R^1 represents a hydrogen atom, an aryl group, a C_{1-5} alkyl group, or a C_{3-6} (total carbon number) alkoxycarbonylalkyl group; R^2 represents a hydrogen atom, an aryloxy group, an arylmercapto group, a C_{1-5} alkyl group or a C_{1-3} hydroxyalkyl group; or R^1 and R^2 are combined with each other to represent C_{3-5} alkylene group; and R^3 represents a hydrogen atom, a C_{1-5} alkyl group, a C_{5-7} cycloalkyl group, a C_{1-3} hydroxyalkyl group, a benzyl group, a naphthyl group, a phenyl group, or a phenyl group substituted with the same or different 1 to 3 substituents selected from the group consisting of a C_{1-5} alkyl group, a C_{1-5} alkoxy group, a C_{1-3} hydroxyalkyl group, a C_{2-5} (total carbon number) alkoxycarbonyl group, a C_{1-3} alkylmercapto group, a C_{1-4} alkylamino group, a C_{2-8} (total carbon number) dialkylamino group, a halogen atom, a trifluoromethyl group, a carboxyl group, a cyano group, a hydroxyl group, a nitro group, an amino group and an acetamide group.

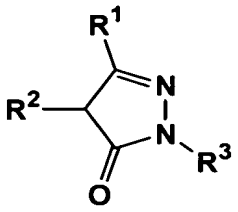
8. (Original) The method according to claim 7 wherein the blood-brain barrier disruption is inhibited by inhibiting increases in permeability of the blood-brain barrier.

9. (Currently Amended) The method according to claim 7 ~~or 8~~ wherein the blood-brain barrier disruption is inhibited by inhibiting increases in the amount of inflammatory cytokines in spinal fluid.

10. (Currently Amended) The method according to ~~any of claims 7 to 9~~ claim 7 wherein the pyrazolone derivative represented by the formula (I) is 3-methyl-1-phenyl-2-pyrazolin-5-one.

11. (Original) A method for preventing and/or treating multiple sclerosis, meningitis, cerebritis or brain abscess which comprises a step of administering to mammals

such as a human, an effective amount of a pyrazolone derivative represented by the formula (I) or a physiologically acceptable salt thereof, or a hydrate thereof or a solvate thereof:

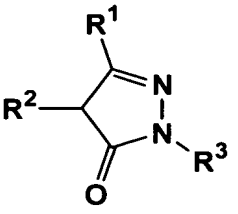


(I)

wherein R^1 represents a hydrogen atom, an aryl group, a C_{1-5} alkyl group, or a C_{3-6} (total carbon number) alkoxycarbonylalkyl group; R^2 represents a hydrogen atom, an aryloxy group, an arylmercapto group, a C_{1-5} alkyl group or a C_{1-3} hydroxyalkyl group; or R^1 and R^2 are combined with each other to represent C_{3-5} alkylene group; and R^3 represents a hydrogen atom, a C_{1-5} alkyl group, a C_{5-7} cycloalkyl group, a C_{1-3} hydroxyalkyl group, a benzyl group, a naphthyl group, a phenyl group, or a phenyl group substituted with the same or different 1 to 3 substituents selected from the group consisting of a C_{1-5} alkyl group, a C_{1-5} alkoxy group, a C_{1-3} hydroxyalkyl group, a C_{2-5} (total carbon number) alkoxycarbonyl group, a C_{1-3} alkylmercapto group, a C_{1-4} alkylamino group, a C_{2-8} (total carbon number) dialkylamino group, a halogen atom, a trifluoromethyl group, a carboxyl group, a cyano group, a hydroxyl group, a nitro group, an amino group and an acetamide group.

12. (Original) The method according to claim 11 wherein the pyrazolone derivative represented by the formula (I) is 3-methyl-1-phenyl-2-pyrazolin-5-one.

13. (Original) Use of a pyrazolone derivative represented by formula (I) or a physiologically acceptable salt thereof, or a hydrate thereof or a solvate thereof, for the production of a blood-brain barrier disruption inhibitor;



(I)

wherein R^1 represents a hydrogen atom, an aryl group, a C_{1-5} alkyl group, or a C_{3-6} (total carbon number) alkoxycarbonylalkyl group; R^2 represents a hydrogen atom, an aryloxy group, an arylmercapto group, a C_{1-5} alkyl group or a C_{1-3} hydroxyalkyl group; or R^1 and R^2

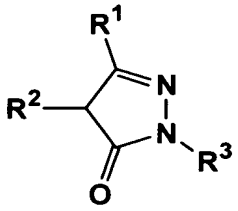
are combined with each other to represent C_{3-5} alkylene group; and R^3 represents a hydrogen atom, a C_{1-5} alkyl group, a C_{5-7} cycloalkyl group, a C_{1-3} hydroxyalkyl group, a benzyl group, a naphthyl group, a phenyl group, or a phenyl group substituted with the same or different 1 to 3 substituents selected from the group consisting of a C_{1-5} alkyl group, a C_{1-5} alkoxy group, a C_{1-3} hydroxyalkyl group, a C_{2-5} (total carbon number) alkoxycarbonyl group, a C_{1-3} alkylmercapto group, a C_{1-4} alkylamino group, a C_{2-8} (total carbon number) dialkylamino group, a halogen atom, a trifluoromethyl group, a carboxyl group, a cyano group, a hydroxyl group, a nitro group, an amino group and an acetamide group.

14. (Original) The use according to claim 13 wherein the blood-brain barrier disruption inhibitor has an action of inhibiting increases in permeability of the blood-brain barrier.

15. (Currently Amended) The use according to claim 13 ~~or 14~~ wherein the blood-brain barrier disruption inhibitor has an action of inhibiting increases in the amount of inflammatory cytokines in spinal fluid.

16. (Currently Amended) The use according to ~~any of claims 13 to 15~~ claim 13 wherein the pyrazolone derivative represented by the formula (I) is 3-methyl-1-phenyl-2-pyrazolin-5-one.

17. (Original) Use of a pyrazolone derivative represented by formula (I) or a physiologically acceptable salt thereof, or a hydrate thereof or a solvate thereof, for the production of a medicament for prevention and/or treatment of multiple sclerosis, meningitis, cerebritis or brain abscess:



(I)

wherein R^1 represents a hydrogen atom, an aryl group, a C_{1-5} alkyl group, or a C_{3-6} (total carbon number) alkoxycarbonylalkyl group; R^2 represents a hydrogen atom, an aryloxy

group, an arylmercapto group, a C_{1-5} alkyl group or a C_{1-3} hydroxyalkyl group; or R^1 and R^2 are combined with each other to represent C_{3-5} alkylene group; and R^3 represents a hydrogen atom, a C_{1-5} alkyl group, a C_{5-7} cycloalkyl group, a C_{1-3} hydroxyalkyl group, a benzyl group, a naphthyl group, a phenyl group, or a phenyl group substituted with the same or different 1 to 3 substituents selected from the group consisting of a C_{1-5} alkyl group, a C_{1-5} alkoxy group, a C_{1-3} hydroxyalkyl group, a C_{2-5} (total carbon number) alkoxycarbonyl group, a C_{1-3} alkylmercapto group, a C_{1-4} alkylamino group, a C_{2-8} (total carbon number) dialkylamino group, a halogen atom, a trifluoromethyl group, a carboxyl group, a cyano group, a hydroxyl group, a nitro group, an amino group and an acetamide group.

18. (Original) The use according to claim 17 wherein the pyrazolone derivative represented by the formula (I) is 3-methyl-1-phenyl-2-pyrazolin-5-one.

19. (New) The blood-brain barrier disruption inhibitor according to claim 2 which has an action of inhibiting increases in the amount of inflammatory cytokines in spinal fluid.

20. (New) The method according to claim 8 wherein the blood-brain barrier disruption is inhibited by inhibiting increases in the amount of inflammatory cytokines in spinal fluid.